REMARKS

I. Applicants' Invention and Preliminary Comments.

Applicants' invention relates to the discovery that harvested bacteria have improved viability (compared with the same bacteria cultured in or grown on a medium not containing resistant starch) if they have been previously cultured in or grown on resistant starch and then subsequently incorporated into a product.

II. Outstanding Rejections

The Examiner has exactly repeated the rejections made in her Office Action of January 21, 2004. Those rejections are as follows:

Claims 41, 76, 77, 79, 81, 88, 90-105, 109-120, 124-135 and 139-150 stand rejected under 35 U.S.C. §102(b) over Masuda et al., U.S. Patent 5,143,845.

Claims 41 and 76-153 stand rejected under 35 U.S.C. §102(b) over Brown et al. U.S. Patent 6,060,050 ("Brown I") in light of evidence of McNaught et al. U.S. Patent No. 5,714,600.

Claims 41 and 76-153 stand rejected under 35 U.S.C. §103(a) in view of Masuda in view of Brown I and McNaught.

Claims 41 and 76-153 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-12 of Brown et al. U.S. Patent 6,221,350 ("Brown III").

III. Patentability Arguments

A. The Rejection of Claims 41, 76, 77, 79, 81, 88, 90-105, 109-120, 124-135 and 139-150 Under 35 U.S.C. §102(b) over Masuda et al. U.S. 5,143,845 Should be Withdrawn.

The anticipation rejection over Masuda et al. should be withdrawn because Masuda fails to disclose each element of the rejected claims. In particular, Masuda fails to disclose the element that the microbes have been cultured in media comprising resistant starch.

The Examiner's suggestion that the claims are inherently anticipated by the culturing method of Masuda Example 2 is incorrect because Masuda makes clear (and those of skill in the art would recognize) that the potato starch compositions of Masuda are cooked in a manner such that no resistant starch would remain. Masuda is directed to a method of preparing microbial cultures on starch media and any of the materials used would be sterilized before their inclusion in the microbial cultures in order to prevent contamination with other cultures. (See Masuda Example 2, col. 2, lines 57-58 which describes autoclaving the basal media.) See also, the Declaration of Ian Brown Under 37 C.F.R §1.132 submitted herewith.

As set out in the Brown Declaration it is well known that potato starch is resistant in its uncooked state but digestible (non-resistant) after cooking. Specifically Rendleman, Biotechnol. Appl. Biochem. 31:171-178 (2000) describes that uncooked potato starch was only 10.9% degraded to G1 to G7 residues after 8 hours in the presence of alpha-amylase. (Table 2) In contrast, potato starch which had been cooked at 100°C for 30 minutes was 88.6% degraded to G1 to G7 residues. (Table 3) Thus, the cooking process of Masuda destroyed the potato starch granule so that the resultant material is no longer RS2 (uncooked starch). Because the residues referred to are small fragments of seven glucose residues or less (the majority contain two (2) glucose units) they are too small to form into RS3 (retrograded starch). See also, Woodruff and Nicoli Starch gels, Cereal Chemistry 8:243 (1931) which teaches the gelatinization temperature of potato starch to be only 69-70°C. Because standard autoclave conditions are the use of 121°C at 15 psig for a minimum of 30 minutes (See Effective Use of Autoclaves: Safety Net #26 - UC Davis Environmental Health and Safety - 2-1493) it is clear that the potato starch components used in the Masuda examples are substantially free of resistant starch. Finally, Raben et al., J. Clin. Nutr. 60: 544-551 (1994) states that raw potato starch has a resistant starch content of about 54% while pregelatinized potato starch comprises 0% resistant starch. The pregelatinized potato starch is simply potato starch that has been cooked in water to completely gelatinize the starch and is dried. For these reasons, it is clear that Masuda fails to anticipate the subject matter of Applicants' claims.

Further, various claims are also novel over the disclosure of Masuda for the additional reasons set out below.

1. Claims 77-78 and 94-108 Define Novel Subject Matter Over Masuda et al.

The anticipation rejection of claims 77-78 and 94-108 under 35 U.S.C. §102(b) over Masuda et al. should also be withdrawn because Masuda et al. do not disclose harvested microbes which have been grown or cultured in a resistant starch of type RS1, RS3, or RS4 much less that such microbes have an increased survival/recovery rate as compared with the same microbes grown or cultured without resistant starch.

2. Claims 79-80 and 109-123 Define Novel Subject Matter Over Masuda et al.

The anticipation rejection of claims 79-80 and 109-123 under 35 U.S.C. §102(b) over Masuda et al. should also be withdrawn because Masuda et al. do not disclose harvested microbes which have been grown or cultured in a resistant starch from rice, barley, wheat, legumes, bananas, or combinations thereof, or that such microbes have an increased survival/recovery rate as compared with the same microbes grown or cultured without resistant starch.

3. Claims 81-87 and 124-137 Define Novel Subject Matter Over Masuda et al.

The anticipation rejection of 81-87 and 124-137 under 35 U.S.C. §102(b) over Masuda et al. should additionally be withdrawn because Masuda et al. do not disclose harvested microbes which have been grown or cultured in a resistant starch derived from a starch having an amylose content of at least 40% (w/w), or that such microbes have an increased survival/recovery rate as compared with the same microbes grown or cultured without resistant starch.

4. Claims 88-93 and 139-153 Define Novel Subject Matter Over Masuda et al.

The anticipation rejection of claims 88-93 and 139-153 under 35 U.S.C. §102(b) over Masuda et al. should further be withdrawn because Masuda et al. do not disclose harvested microbes which have been grown or cultured in a resistant starch that is chemically, physically, and/or enzymatically treated or modified, or the Applicants' discovery that such microbes have an increased survival/recovery rate as compared with the same microbes grown or cultured without resistant starch.

B. The Rejection of Claims 41 and 76-153 Under 35 U.S.C. §102(b) over Brown et al. in view of McNaught et al. should be Withdrawn.

The anticipation rejection of claims 41 and 76-153 under 35 U.S.C. §102(b) over Brown et al. in view of McNaught because Brown et al. should be withdrawn because they do not disclose Applicants' discovery that harvested microbes which have been grown or cultured in a resistant starch have an increased survival/recovery rate as compared with the same microbes grown or cultured without resistant starch. Instead Brown et al. discloses that bacteria grown or cultured by conventional means can better survive in the gastrointestinal tract when they are ingested with resistant starch. (*See* experiment 3 at cols. 11-12). It does not, however, disclose that culturing bacteria with resistant starch outside the gastrointestinal tract can produce a microbial preparation with an increased survival/recovery rate.

Moreover, contrary to the statement at page 10, lines 12-13 of the Office Action, Brown does not teach a microbial preparation "grown on resistant starch." Brown is directed to probiotic compositions comprising bacteria and media for co-administration to subjects and Col. 5, lines 32-36 referred to by the Examiner are directed to Figures 9 and 10 of Brown. These figures depict *in vitro* growth profiles of the probiotic compositions comprising bifidobacteria and clostridia strains with various growth media but do not disclose harvested microbial preparations from a preparatory method.

While it is true that some of the microbes of Brown were "grown" on resistant starch, it was not for the purpose of harvesting the microbes but rather to demonstrate that the resistant starch could function as a growth and/or maintenance media. Regarding col. 7, line 38 of the specification, this paragraph states that resistant starch is added to cell cultures (i.e., the microbes have already been cultured with another cryoprotectant, indicating that resistant starch is being added as a cryoprotectant, not as a culture medium. (Cryoprotectants aid improvements in bacterial recovery during freeze drying by maintaining the viability of the bacterium - these materials are normally low molecular weight sugars, sugar alcohols, and the like. Resistant starch is not a normal cryoprotectant but does seem to maintain the viability of the bacteria.) The paragraph continues that the product is then quickly frozen, which further emphasizes that the resistant starch was not added as a culture medium as it was not given time to act as one.

Moreover, there is no suggestion that microbial preparations be prepared by the method of growing microbes on a resistant starch containing media. There is a distinction between microbes cultured on resistant starch and then put into a product for ingestion and microbes which are a) cultured and then dried with resistant starch; or b) fermented with resistant starch to prove the microbes may use the resistant starch as a Growth or maintenance medium in the GI tract.

The prior art neither discloses nor teaches that culturing the bacteria on resistant starch improves their recovery/survival. Instead it discloses only that the incorporation of resistant starch with microbes in food provides a growth/maintenance medium for the microbes. While not wishing to be bound by a particular theory of mechanism of action it is believed that when bacteria are cultured with resistant starch they use the resistant starch as a carbon source for growth. This increases their robustness and the bacteria are better adapted to utilize resistant starch when they next encounter it as a substrate. While a new "intended use" is insufficient to render a product novel the present rejection is not a lack-of-novelty rejection. (The claimed products are novel for the reasons set out above.) Nevertheless, new properties which are not taught by the prior art are relevant to the issue of non-obviousness under Section 103 and there is no teaching in the art suggesting that one cultivate microbes on resistant starch in order to obtain microbes having improved robustness.

Moreover, there is no disclosure of that aspect of the invention wherein the microbial preparations having an increased survival/recovery rate are combined in a preparation further comprising resistant starch such as recited in claims 78, 80, 82-87, 89 and 151-153. There is no disclosure in Brown to add resistant starch to the microbes cultured on resistant starch. Accordingly, the rejection of those claims should be withdrawn.

C. The Rejection Under 35 U.S.C. §103(a) over Masuda, Brown et al. and McNaught et al. should be withdrawn.

The obviousness rejection of claims 41 and 76-153 under 35 U.S.C. §103(a) over Masuda in view of Brown I and US 5,714,600 (McNaught) should be withdrawn because Masuda, as previously explained, does not disclose microbes cultured on any resistant starch. Masuda discloses that corn starch may be used as a medium, but regular (non-high amylose) corn starch is not significantly resistant. Neither Brown nor McNaught cures the deficiencies of Masuda in that there is nothing in either that would suggest that culturing on resistant

starch would provide any advantages with respect to growth or survival rates. While McNaught teaches that resistant starch may be used in a food product, it does not suggest any advantage of using resistant starch to grow microbes and improve their survival/recovery. Further, one skilled in the art would not combine Brown and McNaught with Masuda to arrive at the intent of the present patent, that is to increase the microbial survival/recovery as there is nothing in any of these patents to show that substituting resistant starch for the corn or potato starch of Masuda would be desired or have such a result.

D. The Rejection Under the Judicially Created Doctrine of Obvious-Type Double Patenting over Brown et al. should be withdrawn.

Finally, the obviousness-type double patenting rejection over claims 1-12 of U.S. Patent No. 6,221,350 should also be withdrawn because claims 1-12 of U.S. Patent No. 6,221,350 are directed to a probiotic composition comprising microorganisms and a resistant starch carrier which acts as a growth or maintenance medium for the microorganisms in the gastrointestinal tract. U.S. Patent No. 6,221,350 neither discloses nor teaches production of a microbial preparation of harvested microbes by culturing on a medium based on or containing resistant starch. Accordingly, the obviousness type double patenting rejection should be withdrawn and each of claims 77-153 should be allowed.

CONCLUSION

For all of the foregoing reasons, the applicants respectfully request that the rejections should now be withdrawn and an early notice of all pending claims is respectfully solicited. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, he is invited to contact the undersigned attorney at the number indicated below.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 13-2855. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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